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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/723,926	11/28/2000	Howard Turner	SMX 3099.11(98-14CIP3DIV2)	7411
321	7590	10/22/2003	EXAMINER SODERQUIST, ARLEN	
SENNIGER POWERS LEAVITT AND ROEDEL ONE METROPOLITAN SQUARE 16TH FLOOR ST LOUIS, MO 63102			ART UNIT 1743	
			PAPER NUMBER	
			DATE MAILED: 10/22/2003	

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n N .

09/723,926

Applicant(s)

TURNER ET AL.

Examiner

Arlen Soderquist

Art Unit

1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 163-171, 178-188 and 190-195 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 180-188 and 190-194 is/are allowed.
- 6) ☒ Claim(s) 163-171, 178, 179 and 195 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 15, 17.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

Art Unit: 1743

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claims 163-171, 178-179 and 195 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lebl in view of Fullemann and Calvet (both newly cited and applied). In the patent Lebl teaches apparatus and method for combinatorial chemistry synthesis. In a first embodiment, this invention includes an integrated robot apparatus for performing combinatorial chemical synthesis protocols and having interchangeable work-stations, robot arm tools, and reaction vessels and reaction vessel arrays. The work-stations and tools are specialized to perform tasks necessary for the synthesis in a plurality of the reaction vessels grouped in a plurality of the reaction vessel arrays. Preferably, these elements function interchangeably because they have standardized sizes and conformation. The work-stations and tools include those for fluid dispensing or aspirating from individual reaction vessels or from all the reaction vessels in an array simultaneously. The reaction vessels can include, alternatively, stackable, ball-sealed reaction vessels, microtitre-like reaction vessel arrays, arrays of independent reaction vessels, valve-sealed reaction vessels (figures 8-11 and the description thereof), septum-sealed reaction vessels (figure 12 and the description thereof), and syringe reaction vessels. In alternative embodiments, this invention includes these work-stations, tools, reaction vessels and reaction vessel arrays in various combinations or sub-combinations either for use in partially integrated robots or for manual or stand-alone use. Column 9, lines 40-54 teach several different examples of the types of compounds which can be synthesized in this manner including

Art Unit: 1743

benzodiazepines. Lebl does not teach that the syntheses occur at elevated pressure, the presence of a catalyst or a closure in which the valve closes prior to the syringe being removed from the device.

In the patent Fullemann teaches a septum for an injection port of a gas chromatograph includes interlocked syringe (103) and duckbill seals (105). The syringe seal prevents fluid leakage during injection by syringe. The duckbill seal prevents fluid leakage after the syringe needle is withdrawn from the septum. A spring clip (107) is used to urge the duckbill closed as the needle is withdrawn. An advantage of this two-component septum is that the duckbill slit can be precisely formed in the duckbill seal before the seals are engaged. Column 1 discusses the problem with typical septum seals including leakage due to seal failure or problems with the syringe due to bent needles. Column 2, lines 40-50 discuss characteristics of duckbill seals including their use as check valves and ability to be used in high-pressure situations. Column 3, lines 44-59 discuss the instant seal, the different functions of the two components and the advantages obtained thereby.

In the patent Calvet teaches process and intermediates for the preparation of benzodiazepines. Column 5 lines 51-64 teaches preparation of benzodiazepines suspending a compound of formula (IV) in 5 to 100 volumes of an organic solvent such as, for example, an lower aliphatic alcohol or an ester of a lower aliphatic alcohol with a lower carboxylic acid, in the presence of a hydrogenation catalyst such as, for example, Raney nickel, rhodium on charcoal or ruthenium on charcoal, which is the reagent generally preferred. The suspension is stirred under a hydrogen atmosphere at a pressure of between atmospheric pressure and 30 atmospheres for a period of between 1 and 50 hours at a temperature of between 0°C and 80 °C.; a pressure slightly above atmospheric pressure, a temperature of approximately 70 °C and a stirring time of 2 hours generally being sufficient to ensure complete the reaction. The reaction medium is then filtered and the catalyst washed several times with a solvent of the same type as that mentioned above. Column 8, lines 1-10 teach an alternate embodiment in which the compound of formula (VI) is combined with a reducing agent in the presence of a reduction catalyst such as, for example, ammonium formate in the presence of palladium on charcoal or hydrogen (under a pressure of between 1 and 5 atmospheres) in the presence of palladium deposited on calcium carbonate (so-called Lindlar catalyst). After filtration of the catalyst, the

Art Unit: 1743

aminated product of formula (V) is isolated in a manner similar to that described above.

Example 1 shows two examples including one in which a reactor capable of withstanding a pressure of 12 bar is used in the process.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a septum with a duckbill valve as taught by Fullemann in the Lebl apparatus and method because of the ability of that septum to provide an effective seal of a pressurized gas during the insertion of a syringe to insert a liquid in the system and the recognition that during the synthesis of compounds such as the benzodiazepines taught by Lebl, elevated pressures would be required as shown by Calvet.

3. Claims 180-188 and 190-194 are allowed. The art of record fails to teach or fairly suggest a method as claimed in which fluids are added to a pressurized reactor through a fluid delivery probe that is inserted into the reactor while the reactor is pressurized.

4. Applicant's arguments filed August 4, 2003 have been fully considered but they are not persuasive. Relative to the apparatus claims examiner points out two things. First the claims are not limited to pressures above ambient and thus include reduced pressures. The claims are also not limited to an particular difference from ambient. As such a device that is capable of introducing fluids at ambient is certainly capable of delivering fluids at pressures near ambient. Second, applicant has missed the discussion of the first method found in column 13 of the Calvet reference in which the suspension of catalyst (Raney nickel) and oxime are introduced into the vessel at a pressure **slightly above atmospheric** pressure. Examiner submits that this shows the knowledge of one of skill in the art to include the knowledge that the pressure should be above atmospheric pressure to prevent the mixture from contacting the ambient atmosphere possibly to prevent problems with the reaction due to contact with water or oxygen that are inherently in the ambient atmosphere. This would be carried over to the second method found in column 14. Additionally one of skill in the art would have recognized that inclusion of the valve of Fullemann would have allowed the elimination of the need to repressurize the system as it is capable allowing fluidic access at reaction pressure. Thus either way a pressure different from ambient is suggested by the Calvet reference because of a recognition as outlined above.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


Art Unit: 1743

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (703) 308-3989. The examiner's schedule is variable between the hours of about 5:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

For communication by fax to the organization where this application or proceeding is assigned, (703) 305-7719 may be used for official, unofficial or draft papers. When using this number a call to alert the examiner would be appreciated. Numbers for faxing official papers are 703-872-9310 (before finals), 703-872-9311 (after-final), 703-305-7718, 703-305-5408 and 703-305-5433. The above fax numbers will generally allow the papers to be forwarded to the examiner in a timely manner.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.



October 20, 2003

ARLEN SODERQUIST
PRIMARY EXAMINER